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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,685	MI ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-78,80,81 and 100* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-78,80,81 and 100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office Action is in response to the paper filed April 21, 2009.

Claims 58-78, 80, 81, and 100 are currently pending and are under examination. In the previous Office Action, the broadest claims were examined, and art found that anticipated or rendered obvious these claims and those limited to amino acids 454-458 of SEQ ID NO: 2 and the encoding polynucleotides. Thus, in accordance to the restriction requirement, only SEQ ID NO: 2 and amino acids 454-458 of SEQ ID NO: 2 have been searched.

Benefit of priority is to March 19, 2003.

Note that Sp35 is known as LINGO andLINGO-1 in the prior art. See specification at page 2 line 26-27.

Withdrawal of Objections:

The objection to the disclosure because this application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b) is withdrawn.

Maintenance of Rejections:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 63 is again rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 63, nucleic acids encode proteins, but whether the protein is cyclic or not is a post-translational event.

Applicants assert that nucleic acids encoding cyclized polypeptides can be created by adding nucleotides encoding cysteines to the termini of the polynucleotide sequence and therefore Claim 63 is definite. The placement of nucleic acid encoding cysteines at the termini of the polynucleotide sequence results in a nucleic acid encoding polypeptide having cysteines at each termini. The disulfide bond that may form between the two terminal cysteines is a post-translational event having nothing to do with the encoding nucleic acid.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 58, 59, 64-66, 69, and 70 are again rejected under 35 U.S.C. 102(b) as being anticipated by Osada et al. (2001; Assignment of 118 novel cDNAs of cynomolgus monkey brain to human chromosomes. Gene. 275: 31-37).

Osada et al. teach nucleic acid encoding LINGO-1 (Table 1, AB046639) derived from cynomolgus monkey. LINGO-1 differs from instant SEQ ID NO: 2 at Ser527Pro. Therefore, LINGO-1 amino acids 1-526 or 528-614 are fragments of SEQ ID NO: 2.

Therefore, Osada et al. teach an isolated nucleic acid encoding a soluble fragment of SEQ ID NO: 2 (**Claim 58**), wherein the nucleic acid encodes amino acids 454-458 of SEQ ID NO: 2 (**Claim 59**j).

At page 32, left col., last sentence at para 2.2, the cDNA was placed into plasmid pME18S-FL3 (**Claim 65, 66**) and these plasmids where transformed into host cells (**Claim 69, 70**).The making of plasmids and electroporation of cells requires compositions comprising water. Therefore, Osada et al. teach a composition comprising a polynucleotide encoding amino acids 454-458 of SEQ ID NO: 2 and a pharmaceutically acceptable carrier (**Claim 64**).

Applicants urge that the protein described by Osada et al. contains a transmembrane domain and is not soluble. Applicants urge that Osada et al. do not disclose any fragments of LINGO-1.

In response, the claims include the term "comprising". Therefore, Osada et al. teach a nucleic acid *comprising* (reads on full-length LINGO-1) nucleic acid encoding the soluble fragment of 454-458 of SEQ ID NO: 2.

It is admittedly difficult to claim a nucleic acid encoding only a specific fragment of a peptide because "comprising" and "encoding" language is considered to be open language. Applicants may wish to consider the following claim language when amending their claims:

Example 1:

Isolated nucleic acid consisting of nucleotides X to Y of SEQ ID NO: Z which encodes amino acids 454-458 of SEQ ID NO: 2.

Example 2:

Isolated nucleic acid consisting of nucleotides encoding only amino acids 454-458 of SEQ ID NO: 2.

Vectors are another issue that must be dealt with carefully. If Applicants were to draft a claim such as shown in Example 1 above, the placement of this nucleic acid into a vector would again read on Osada et al.'s vector. For example:

Example 3:

A vector *comprising* a nucleic acid consisting of nucleotides X to Y of SEQ ID NO: Z.

The open language allows there to be any nucleotide sequence 5' or 3' to the specific nucleotides X to Y. Thus, the vector comprising nucleic acid encoding LINGO-1 as taught in Osada et al. would read on the vector exemplified in Example 3. Possible language that may thwart such a rejection is exemplified below:

Example 4:

A vector comprising a nucleic acid consisting of nucleotides X to Y of SEQ ID NO: Z, wherein said nucleic acids X to Y of SEQ ID NO: Z are flanked by heterologous sequences.

OR

Example 5:

A vector comprising a nucleic acid consisting of nucleotides X to Y of SEQ ID NO: Z, wherein said nucleic acids X to Y of SEQ ID NO: Z are flanked by heterologous sequences, wherein the expression of said vector results in the production of a polypeptide consisting of amino acids 454-458 of SEQ ID NO: 2.

Please be careful not to add new matter to the disclosure.

Claims 58-78, 80, and 100 are again rejected under 35 U.S.C. 102(b) as being anticipated by Jacobs et al. (1998; USP 5,707,829).

Jacobs et al. teach SEQ ID NO: 6 comprising amino acids 454-458 of instant SEQ ID NO: 2 at amino acids 65-69 of Jacobs et al. SEQ ID NO: 6. Jacobs et al. nucleotides 268-283 of SEQ ID NO: 5 encodes Jacobs et al. amino acids 65-69 of SEQ ID NO: 6.

Therefore, Jacobs et al. teach an isolated nucleic acid encoding a fragment of instant SEQ ID NO: 2 (**Claim 58**), wherein that fragment is amino acids 454-458 of SEQ ID NO: 2 (**Claim 59**p).

At Col. 6, line 21-30, Jacobs et al. teach to fuse fragments of SEQ ID NO: 6 to carrier molecules such as immunoglobulins and particularly IgFc. At Col. 7, line 27+, Jacobs et al. teachto express the protein in a form which will facilitate purification, such as with epitope tags. (**Claims 60, 61, 62**)

At Col. 6, line 17, Jacobs teach to cyclize fragments of SEQ ID NO: 6 (**Claim 63, 73**).

At Col. 6, line 31+, Jacobs et al. teach to place the polynucleotide sequence SEQ ID NO: 5 into a vector (**Claim 65, 66**) and at line 45+ teach to express the protein in suitable host cells (**Claim 69, 70, 100**).This method of placing nucleic acid into plasmids and transforming host cells with the plasmid requires compositions comprising water, for example. Therefore, Jacobs et al. teach a composition of nucleic acid SEQ ID NO: 5 in a pharmaceutically acceptable carrier (**Claim 64**). Therefore, Jacobs et al. teach isolated polypeptides comprising fragments of SEQ ID NO: 2 and comprising amino acids 454-458 of SEQ ID NO: 2 (**Claim 71, 72**). At Col. 7, the protein may be produced by operatively linking the encoding polynucleotide into a baculovirus/insect expression system (**Claim 67, 68**).

Pharmaceutical compositions of protein are set forth at Col. 16, line 25+ (**Claim 80**). At Col. 20, line 9, the polypeptide can be placed with co-polymers such as polyethylene glycol (**Claim 74-78**).

Applicants urge that Jacobs et al. does not teach that L105 encodes a protein capable of decreasing the inhibition of axonal growth in a CNS neuron. Applicants are

first referred to the responses above regarding nucleic acid and "comprising" language, which appears to be the stumbling language that is resulting in these art rejections. Because your elected amino acid sequence 454-458 of SEQ ID NO: 2 is found to be encoded by L105 of Jacobs et al., that sequence must have the property of decreasing the inhibition of axonal growth in a CNS neuron.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 58, 69, 70, 71, 72, 80, and 100 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Osada et al. (2001; Assignment of 118 novel cDNAs of cynomolgus monkey brain to human chromosomes. Gene. 275: 31-37).

The teachings of Osada et al. are set forth above. Osada et al. teach the deduced amino acid sequence of LINGO-1, which differs from instant SEQ ID NO: 2 at Ser527Pro. Therefore, LINGO-1 amino acids 1-526 or 528-614 are fragments of SEQ ID NO: 2. Osada et al. do not teach the isolated LINGO-1.

Osada et al. teach that the cDNA of Old World monkeys are highly similar to that of the human genome at the molecular level (page 32, left col., top) and that these cDNAs maybe used to isolate novel genes encoding protein in humans (Abstract; page

31). Osada et al. teach that LINGO-1 has many motifs such as the dyhydrogenase/reductase signature, connexin signature 1, EGF-like domain signature 2, and calcium binding EGF domain signature pattern (Table 2; F6, F17, F24, F25).

It would have been obvious for a person having ordinary skill in the art to use the host cells of Osada et al. to recombinantly produce the LINGO-1 protein comprising a fragment of SEQ ID NO: 2 and amino acids 454-458 of SEQ ID NO: 2 (**Claim 58, 71, 72**) and isolate the protein therefrom (**Claim 69, 70, 100**) because Osada et al. teach that this protein has many recognized signature motifs in humans and may further elucidate the potential of human genes and proteins. Cell culture medium and compositions used to isolate proteins comprise water. Therefore, compositions comprising polypeptides comprising fragments of SEQ ID NO: 2 or fragments comprising 454-458 of SEQ ID NO: 2 and a pharmaceutically acceptable carrier is obvious (**Claim 80**).

Applicants opine that one of ordinary skill in the art would not have arrived at Applicant's claimed invention with any sort of predictability whatsoever and assures the Examiner of the teachings of KSR. As noted in the rejection, motivation, suggestion, and predictability are set forth in Osada et al. The burden shifts to the Applicants to demonstrate that the invention as claimed is not predictable over the teachings of Osada et al.

Claims 58, 59, 64-66, 69, 70, 71, 72, 80, and 100 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Osada et al. (2001; Assignment of 118 novel cDNAs of cynomolgus monkey brain to human chromosomes. Gene. 275: 31-37).

The teachings of Osada are set forth above in the rejections under 35 USC 102(b) and 103.

As noted in the restriction requirement, Applicants may elect a single sequence to represent all or a subset of claimed sequences. Applicants elected amino acids 454-458 of SEQ ID NO: 2 and encoding polynucleotide to represent the subset of polynucleotides and amino acids sequences of Claim 59a-k, as applied to elected Group 1, Claims 58-78, 80, 81, and 100. Therefore, in accordance to Applicant's election, all of the fragments of SEQ ID NO: 2 listed in Claim 59a-k are obvious variants of polynucleotides encoding amino acids 454-458 of SEQ ID NO: 2 and polypeptides comprising 454-458 of SEQ ID NO: 2 as applied to the teachings of Osada et al.

Applicants have not presented arguments regarding this rejection.

Claims 58-78, 80, and 100 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobs et al. (1998; USP 5,707,829).

The teachings of Jacobs et al. are set forth above.

As noted in the restriction requirement, Applicants may elect a single sequence to represent all or a subset of claimed sequences. Applicants elected amino acids 454-458 of SEQ ID NO: 2 and encoding polynucleotide to represent the subset of

polynucleotides and amino acids sequences of Claim 59a-k, as applied to elected Group 1, Claims 58-78, 80, 81, and 100. Therefore, in accordance to Applicant's election, all of the fragments of SEQ ID NO: 2 listed in Claim 59a-k are obvious variants of polynucleotides encoding amino acids 454-458 of SEQ ID NO: 2 and polypeptides comprising 454-458 of SEQ ID NO: 2 as applied to the teachings of Jacobs et al.

Applicants opine that one of ordinary skill in the art would not have arrived at Applicant's claimed invention with any sort of predictability whatsoever. As noted in the restriction requirement:

Additionally, there are 20 different variants of SEQ ID NO: 2 listed in Claim 59. **Applicants must elect a single variant for search, OR Applicants must provide a single sequence or subsequence** that will represent a subset of, or all of, the 20 different variants of SEQ ID NO: 2 listed in Claim 59. This is not a species election but an election of an invention because the variants differ in structure and cannot be searched via a single polypeptide or nucleic acid sequence search.

Applicants elected nucleic acid encoding amino acids 454-458 of SEQ ID NO: 2 to represent a subsequence of the variants listed in Claim 59. Therefore, art anticipating this elected fragment renders obvious all of the variants listed in the claims.

New Objections and Rejections:

The claim set is objected to because of the following informalities: Applicants have not referred to Claims 1-57 as having been cancelled. Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 59g is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 59g refers to a polypeptide comprising a transmembrane domain. Transmembrane domains are not soluble proteins as Applicants have noted themselves in their response at page 11, para. 1 and page 15, penultimate sentence.

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen Cochrane Carlson/
Primary Examiner, Art Unit 1656